

Award Number: DAMD17-02-2-0006

TITLE: Center for Integration of Medicine and Innovative Technology

PRINCIPAL INVESTIGATOR: John A. Parrish, M.D.

CONTRACTING ORGANIZATION: The Massachusetts General Hospital Corporation  
dba Massachusetts General Hospital  
Boston, MA 02114

REPORT DATE: November 2008

TYPE OF REPORT: Final

PREPARED FOR: U.S. Army Medical Research and Materiel Command  
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;  
Distribution Unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

REPORT DOCUMENTATION PAGE				Form Approved OMB No. 0704-0188	
Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Department of Defense, Washington Headquarters Services, Directorate for Information Operations and Reports (0704-0188), 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to any penalty for failing to comply with a collection of information if it does not display a currently valid OMB control number. PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ADDRESS.					
1. REPORT DATE 1 Nov 2008		2. REPORT TYPE Final		3. DATES COVERED 1 Oct 2001 – 31 Oct 2008	
4. TITLE AND SUBTITLE  Center for Integration of Medicine and Innovative Technology				5a. CONTRACT NUMBER	
				5b. GRANT NUMBER DAMD17-02-2-0006	
				5c. PROGRAM ELEMENT NUMBER	
6. AUTHOR(S)  John A. Parrish, M.D.  E-Mail: <a href="mailto:mlender@partners.org">mlender@partners.org</a>				5d. PROJECT NUMBER	
				5e. TASK NUMBER	
				5f. WORK UNIT NUMBER	
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)  The Massachusetts General Hospital Corporation dba Massachusetts General Hospital Boston, MA 02114				8. PERFORMING ORGANIZATION REPORT NUMBER	
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012				10. SPONSOR/MONITOR'S ACRONYM(S)	
				11. SPONSOR/MONITOR'S REPORT NUMBER(S)	
12. DISTRIBUTION / AVAILABILITY STATEMENT Approved for Public Release; Distribution Unlimited					
13. SUPPLEMENTARY NOTES					
14. ABSTRACT  The Center for Integration of Medicine and Innovative Technology (CIMIT), is a consortium of nonprofit Massachusetts-based institutions led by Massachusetts General Hospital and includes Brigham and Women's Hospital, Massachusetts Institute of Technology and Draper Laboratory. CIMIT develops technologies to advance the diagnosis and treatment of patients using minimally invasive and less costly approaches. CIMIT coordinates and implements research programs in cardiovascular disease, cancer, trauma, and critical care, supported by basic science and engineering development in biomaterials, endoscopic tools, energy delivery, medical imaging, and other novel technologies. This unique military/civilian partnership allows DoD the transfer to the military of successful minimally invasive approaches developed at CIMIT. The overall goal of CIMIT is to create a national program that combines clinical and technological excellence and educational components to generate, develop, and reduce-to-practice innovative and high-impact concepts in minimally invasive therapy.					
15. SUBJECT TERMS Not Provided					
16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			USAMRMC
U	U	U	UU	13	19b. TELEPHONE NUMBER (include area code)

**CIMIT Annual Report for DAMD17-02-2-0006****Oct. 1, 2007 to Sept. 30, 2008**

<b><i>Principal Investigator</i></b>	<b><i>Title</i></b>	<b><i>Page</i></b>
Chen	Restraint: Therapy for Ischemic Mitral Regurgitation	4
Fauza	Optical enhancement in videofetoscopy	5
Harris	The Development of a Comprehensive Patient Care Station - Final Report	7
Whitesides	Microfluidic Device for Low-Cost Screening of Newborns for Severe Combined Immune Deficiency (SCID)	11
Yelick	Composite Titanium/bioengineered Dental Tissue Implants – Final Report	12

# Quantitative Ventricular Restraint: Therapy for Ischemic Mitral Regurgitation

Frederick Chen, MD, PhD, Principal Investigator

CIMIT Project # 07-003

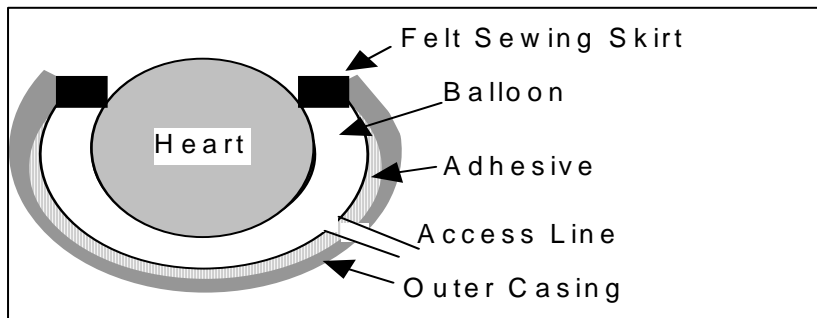
Quarter Ending September 30, 2008

## Overall Goals and Approach

Ventricular restraint is a novel treatment modality for heart failure that has demonstrated effectiveness in reducing ventricular size. We have developed a novel device that allows the application of ventricular restraint in a quantitative and adjustable manner (see Figure below) and previously shown that reduction in ventricular size is intimately related to restraint level.

Ischemic mitral regurgitation is the result of dilatation of the ventricle. As the ventricle dilates and pulls on the leaflets, the leaflets ultimately separate, causing a failure of leaflet coaptation. Currently, treatment of such mitral regurgitation involves either mitral valve ring annuloplasty or mitral valve replacement.

The overall goals of this project are to 1. Reproduce a large animal model of ischemic MR and 2. Demonstrate that utilization of our device to reduce ventricular size will ameliorate such MR. This approach utilizes a half ellipsoid fluid-filled balloon to completely envelop the ventricles. We have developed this device from prototype form to a medical grade device to test in sheep.



## Progress This Past Quarter

This past quarter we successfully implanted the restraint device for the first time in an animal with MR. We will follow this animal by serial echo to see if the MR decreases as reverse remodeling progresses.

We will continue to implant more animals with the device.

I appreciate the support of CIMIT in this important research effort.

# Optical Enhancement in Videofetoscopy

Dario Fauza, MD, Principal Investigator

CIMIT Project # 06-015

Quarter Ending September 30, 2008

## Overall Goals and Approach

Current videofetoscopic techniques demand the replacement of the amniotic fluid with an optically neutral solution, such as Ringer lactate or normal saline, due to the limited light diffusion and poor visibility of the fetus through the amniotic fluid. Such replacement can lead to complications such as dissection of the gestational membranes, infection, and preterm labor. Originally, we proposed to initiate the development of a digital video system that would preclude the need for amniotic fluid exchange during videofetoscopy.

First, we had to measure the precise optical properties of the amniotic fluid at different gestational ages and thus be able to determine the optimal light wavelength for penetration through the fluid. It is well known that, in order to obtain maximum transmitted signal, an “impedance” adaptation of the complete optical system is needed between the light source, the receiving camera and the propagation medium – in this case, the amniotic fluid.

In a second phase of the study, digital image-based rendering manipulations were to be developed, in order to filter/enhance the video image in real time and hopefully eliminate the need for amniotic fluid exchange.

## Progress This Past Quarter

After some quite protracted freezing, the funds for this project were made available only in mid-2007. Since then, we have completed the first phase of the project, namely the optical analysis of the amniotic fluid at different gestational ages, as detailed in a previous report. This was a study in and of itself, which was presented before the “Third Annual Academic Surgical Congress”, in Huntington Beach, CA, in February of this year. The formal title of the presentation was: “Steigman SA, Kunisaki SM, Wilkins-Haug L, Takoudes TC, Fauza DO. Optical properties of human amniotic fluid: implications for videofetoscopic surgery.” A related original manuscript is being prepared for submission. As to progress on the second phase of the project, please see below.

## Patent Activity

The perspective of a partnership with the industry, as described above, hinges on an agreement between Children's Hospital Boston's Intellectual Patent Office (IPO) and OTI, currently under review by both parties. Should such an agreement be reached, new intellectual property is expected and indeed somewhat of a pre-requisite for OTI to engage in this collaboration. Regarding intellectual property related to optical hardware development, as per a recent report, a fairly extensive patent search by a patent attorney hired by the hospital's IPO turned out negative.

This has led to a decision by the hospital's IPO to file for a provisional patent application of such a device. A definitive patent application would hinge on the generation of a working prototype, which would also depend on the formal establishment of the partnership with OTI.

# The Development of a Comprehensive Patient Care Station – Final Report

Bette Ann Harris, DPT, MS, Principal Investigator

CIMIT Project # 04-088

Quarter Ending June 30, 2008

## **Overall Objectives and Approach**

The focus of the project is to consolidate the bedside assistive and adaptive equipment into a comprehensive unit that promotes patient independence and safety and reduces the physical burden on caregivers. The patient care station has two components: the chair with the transfer bridge and a canopy having 2 parts: bed canopy and chair canopy.

New design of hospital rooms: The present rooms in the hospital are built assuming that the patient will not be ambulatory, but the therapists work to get the patient out of the bed and mobile. The 'future hospital room' or the 'room for the future' would be a single-bed room with standardized, automated equipments in all rooms and for all patients.

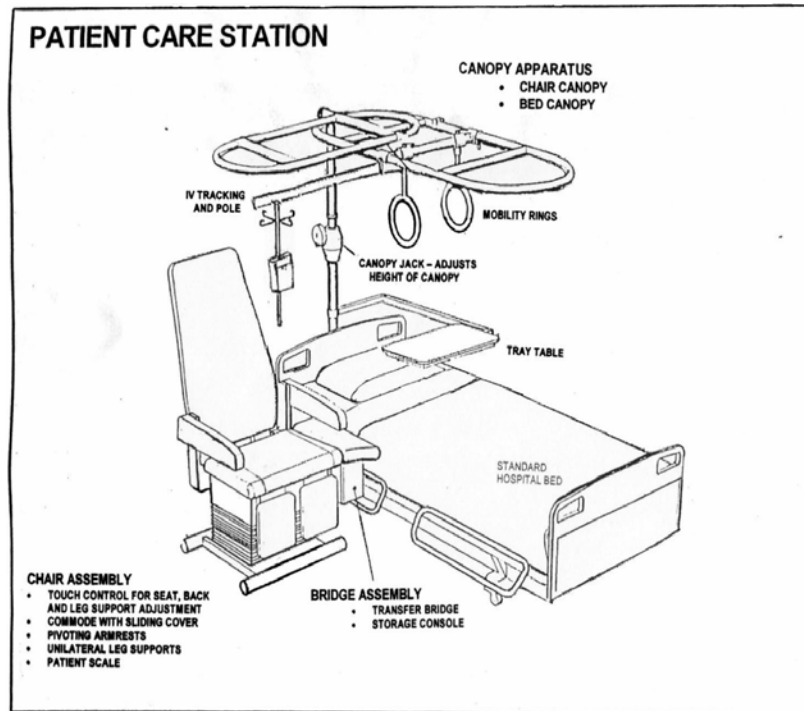
The 'no lift policy' that is coming to effect, as in the state of Washington about no-lifting of patients by nurses, to reduce work-related musculoskeletal injuries to the caregivers would require a transfer system which would allow the patients to be mobile and independent with minimal assistance.

## **Summary of Results since the last report**

In October, we participated in the Exploratorium at the Annual CIMIT conference as well as the Coming of Age invited conference for nursing. At both events, we received positive feedback on our concept design and met potential vendors who may be willing to build both the prototype and market the chair. We have written to these companies and now, we will follow up with individual meetings. We are also discussing additional strategies to get to this next step with both Janice Crosby and Ann Humphries. We are hopeful that in the next few months we will have a commitment from one of our prospects to proceed with building a chair that can be tested on potential users.

## Progress on Specific Aims

Proposed solution:



### Features and advantages:

#### Chair Base:

Includes a chair/commode, providing a level surface for transfers enabling patient independence in self-care.

Adjustable seat height accommodates patients from 5'0" to 6'5.

The entire base including the seat is able to tilt backwards, preventing patients from sliding out of the chair.

Telescoping leg rests, separate for each leg, allow for patients to keep one/both legs elevated for comfort, to reduce swelling, facilitate circulation and reduce pain.

Pivoting arm rests enable an easy transfer to or from the chair to the transfer bridge or the bed onto either side.

#### Chair Back:

Traversing seat back and arm rests accommodate a wide range of patient sizes and shapes.

Reclining seat back provides comfort and pressure relief and optimal patient positioning.

#### Transfer Bridge:



Can be attached to either sides of the chair to facilitate transfer to the bed/wheelchair from either side of the chair.

Storage box underneath the surface of the bridge provides storage for personal belongings, reducing clutter in the room.

**Bed & Chair Canopy:**

Canopy has 2 parts: bed canopy and chair canopy, which can be swung over the bed and chair when needed, providing overhead assistance for bed to chair/chair to bed transfers.

Canopies have mobility rings, with which patient can reposition him/herself in bed, or assist in coming from lying down to sitting.

**Canopy Base:**

Adjustable tray table provides access; serves as a source for TV/internet/electric power/personal items.

IV tracking pole allows bedside transfers and easier access without any restrictions; increases space in the room.

**Publications and Presentations**

Exploratorium exhibitor; '07 CIMIT Innovation Conference

**Proposal Activities**

Next Steps:

- Build a patient care station that is reasonably priced, stable, would not compromise patient safety, and is mobile, which can be easily moved out of the way; a chair that has multiple utilities like a bedside commode and has motorized operation so that it can be easily operated by the patient and all care-givers with minimal assistance.
- Pilot test the prototype with appropriate patients.

Schedule some type of presentation with potential funders and manufacturers, after guidance from CIMIT leaders.

**Issues and Concerns**

Without a commitment from a vendor to build a workable patient care station, we would need to seek additional funding in order to proceed. Perhaps finding a partner who we can submit a SBIR grant would be an alternative plan.

As always, time is our biggest challenge. Because of the change in leadership at the MGH Institute of Health Professions, I am now serving as the Interim Associate Academic Dean as well as getting a new Randomized Clinical Trial organized to go into the field this summer (the Effectiveness of the Strong for Life Program for Patients Post Hip Fracture Rehabilitation; funded from NINH R01

Partnership grants with Spaulding Rehabilitation Hospital and the Health and Disability Research Institute, Boston University of Public Health.)

This report reminds me that I need to make time to work with my colleagues (Kath Harney and the people at CIMIT) to pull together potential manufacturers for a meeting. We have done some work, in preparing for this including developing a brochure and preparing letters for CIMIT. Our goal is to accomplish this late spring. I remain committed to the grant as I believe the ultimate product will clearly improve patient care. On June 4, 2008, I participated in a CIMIT sponsored dinner *Making a Difference: Connecting Innovators in Elder Care* and will follow up with some new contact. We need the help from CIMIT staff (Janice Crosby has had us get in touch with Anne Humphrey) in order to have a professional plan to entice a partner or manufacturer. Unfortunately, we have not made any substantial progress since our last report due to time constraints but are still hopefully that we can find a company interested in testing a prototype and ultimately, marketing the Chair.

# Microfluidic Device for Low-Cost Screening of Newborns for Severe Combined Immune Deficiency (SCID)

George M. Whitesides, PhD, Principal Investigator

CIMIT Project # 06-067

Quarter Ending September 30, 2008

## Overall Objectives

SCID is a group of life-threatening genetic disorders characterized by extreme susceptibility to infection because of profound T cell failure. Currently, patients are diagnosed with SCID after 6-8 months, and as a result have compromised survival despite hematopoietic stem cell transplantation. Diagnosis at birth, on the other hand, allows for nearly 100% survival. Universal screening of infants for this sporadic disorder can save lives, but current diagnostic tests are too expensive (~ \$100-\$1000 / child) for broad screening. Our goal is to develop a \$1 test to enable universal screening for this serious primary immunodeficiency.

In this proposal, we are developing a diagnostic tool that allows low-cost and rapid detection of T cells to screen for SCID. The kit has two parts: a disposable microfluidic channel that captures and processes blood, and a detector that interrogates the channel for the presence of T cells. Both aspects of the kit are intended to be low-cost, built from simple technologies developed in the Whitesides Lab.

## Quarterly Status Report

We are currently making progress in the development of the low-cost photodetector device to interrogate the presence of labeled T cells in the microfluidic channel.

**Detector:** We have switched our light source to a low-cost red laser to improve light throughput. We are currently working on aligning the cartridges reproducibly so that the light source and detectors are aligned.

**Channel:** We have developed microfluidic channels that enable capture of T cells from a drop of blood. These channels are prototyped from the transparent, elastomeric polymer polydimethylsiloxane.

**Present Plans:** The detector is being reconfigured with a method to reliably align the cartridge, so that the fiber optics on the cartridge will align with the laser source and detector. We will then calibrate the detector with adult whole blood samples. To correlate detector values, the absolute count of T cells in the blood specimens will be determined by flow cytometry. Upon calibration with these clinical samples, we will program the detector to flag specimens with T cell counts less than 1200 cells/ $\mu$ L, which was shown to adequately capture all SCID patients in a large series (Buckley, et al., J Peds 1997).

# Composite Titanium/bioengineered Dental Tissue Implants – Final Report

Pamela Yelick, PhD, Principal Investigator

CIMIT Project # 06-061

Quarter Ending September 30, 2008

## Overall Goals and Approach

To bioengineer anatomically correct tooth root tissues on scaffold sleeve covered titanium surfaces grown in the mandible.

**Milestone #1.** Demonstrate the formation of cementum on titanium implant surfaces grown in the mandible.

**Milestone #2.** Demonstrate the formation of cementum and periodontal ligament on titanium implant surfaces grown in the mandible.

**Milestone #3.** Demonstrate the formation of cementum, periodontal ligament, and alveolar bone on titanium implant surfaces grown in the mandible.

## Progress This Past Quarter

Implant status. All harvested implants have now been analyzed.

Molecular/Cellular and differentiative characterizations. We have completed the molecular and cellular characterizations for all harvested cell populations.

Analysis of the Ti/bioengineered PDL tissue interface. We have completed analysis of all of the harvested implants.

## Issues or Concerns

We are in the process of finalizing our results and discussion, and will submit this manuscript within the next few weeks.

## Patent Activity

As stated in our last report, have submitted provisional patents to Tufts University, through Dr. John Cosmopoulos, of the IP team here at Tufts University. We are focusing on the methods used to harvest, culture, and seed the PDL cells onto the scaffold coated titanium implant.

## Proposals and Awards

I have included these results in a competing renewal R01 grant application, which was submitted in July. This grant has not yet been reviewed, but will likely be within the next few weeks.

## Publications/presentations/patents

Dr. Yan Lin presented this work in an oral presentation at the International Association for Dental Research in Toronto this past July.

### **Current Status**

We anticipate manuscript submission by mid November.

### **Next steps**

We anticipate combining this PDL tissue engineering approach with novel dental tissue engineering scaffolds, to improve our model for bioengineered PDL tissue regeneration. We are investigating the possibility of fabricating hybrid scaffolds for tooth root and periodontal ligament tissue engineering, in collaboration with the laboratories of Dr. David Kaplan, Tufts University, and Dr. John Jansen, from the University of Nijmegen, The Netherlands.